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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,498	05/15/2001	John E. Sims	0317-US	8629

22932 7590 02/06/2003

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 02/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Rk copy

Office Action Summary	Application No. 09/763,498	Applicant(s) Sims et al.
	Examiner Fozia Hamud	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 13, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *21-44* is/are pending in the application.

4a) Of the above, claim(s) *40-43* is/are withdrawn from consideration.

5) ☒ Claim(s) *24, 27, 30, 34, and 39* is/are allowed.

6) ☒ Claim(s) *21-23, 25, 26, 28, 29, 31-33, 35-38, and 44* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Office Action

1. Receipt of Applicants' arguments and amendments filed in Paper No.11 on 13 November 2002 is acknowledged. Claims 21-35, 38-39 have been amended and new claim 44 has been added. Thus claims 21-44 are pending.

Restriction Requirement:

2. Applicants traverse the restriction between Group I (claims 21-39), drawn to an isolated nucleic acid molecules, Group II (claims 40, 42), drawn to an antibody that binds to the polypeptide of SEQ ID NO:8, and Group III (claims 41, 43), drawn to an antibody that binds to the polypeptide of SEQ ID NO:13. Applicants submit the same traversal as set forth in their Response to Restriction Requirement, which was based on the premise that the nucleic acid molecules of SEQ ID Nos: 7 and 12 are structurally similar and that the nucleic acid molecules of SEQ ID NO:5 are contained fully within the nucleic acid of SEQ ID NO:7, therefore, there are no basis for restricting these nucleic acid molecules, and that Annex B Unity of Invention (PCT/AI/1 Rev.1), Example 17, which describes that unity between a protein X and the DNA encoding it.

Applicants' traversal is not deemed persuasive, because it does not apply to the instant restriction for the following reasons.

As was set forth in the restriction requirement mailed on 24 January 2002 in Paper NO:8, page 4, pursuant to 37 C.F.R. 1.475(d), this Authority considers that the main invention in the instant application comprises the first-recited product, drawn to an isolated nucleic acid molecules, encoding the polypeptide of SEQ ID NO:6, 8 or 13, said nucleic acid molecules comprising the

nucleotide sequences set forth in SEQ ID NO:5, 7 and 12 respectively, an expression vector comprising said nucleic acids, a host cell comprising said vectors, a method of producing the polypeptide of SEQ ID NO:6, 8 or 13 and the polypeptide of SEQ ID NO:6, 8 or 13, and the first-recited method of using that product, namely in the process of producing the encoded polypeptide. Note that there is no method of making the polynucleotide. Further, pursuant to 37 C.F.R. 1.475(b)-(d), the ISA/US considers that the materially and functionally dissimilar products of group II -III do not correspond to the main invention. This Authority therefore considers that the several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 40-43 stand withdrawn from consideration by the Examiner as they are drawn to non-elected inventions.

Response to Amendment:

3. The following previous objections and rejections are withdrawn in light of Applicants amendment filed on 02 July 2002 in Paper No.9:

(I) The objection of claims 21-23, 26-32 and 39.

(II) The rejection claims 24-25, 32-35 made under 35 U.S.C.§101.

(III) The rejection of claims 21-23, 26, 29, 36-38 made under 35 U.S.C. 112, second paragraph.

Claim rejections-35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

> and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 21-23, 26, 29, 36-37, 38 stand rejected under 35 U.S.C. 112, first paragraph, for reasons of record set forth in the office action mailed on 02 July 2002, in Paper NO:9, pages 4-6.

Applicants argue that in the art of molecular biology the level of the ordinary skill is high and knowledge of sophisticated techniques and method are presumed. Applicants submit that instant specification discloses sequence information for murine and human IL-1 epsilon and describes assays for determining if an IL-1 epsilon polypeptide or fragment thereof retains activity as claimed. Applicants further submit that it requires only routine methodology to construct a DNA that encodes a polypeptide that is a fragment of an IL-1 epsilon and to test whether said fragment retains activity in IKBα or p38MAP kinase phosphorylation or in cell surface expression of ICAM-1. Furthermore, instant claims recite an operable activity, which further limits the claims. Applicants argue that there is nothing in the law that requires that specification identifies specific fragments that retain activity, only that the skilled artisan is able to practice the claimed invention without undue experimentation. Thus, instant specification in combination with the knowledge of those skilled in the art, how to make IL-1 epsilon and test them for the recited activities, is enabled.

Applicants' arguments have been considered fully but are not deemed persuasive. Although the level of the ordinary skill in molecular biology is high, the predictability of the art, the number of working examples, as well as the guidance presented in the instant specification and the state of the prior art of record, are also to be considered when determining undue experimentation. Instant specification does not teach which regions of the claimed polypeptide are critical for the functional integrity of the protein. The specification does not provide the requisite

examples nor a representative number of different fragments of the IL-1 epsilon that retain the recited activities, nor does the disclosure provide criteria that explicitly enable such critical features. **To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application, regardless how sophisticated the available techniques might be, but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed IL-1 epsilon, which are required for functional and structural integrity of the protein. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a fragment which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.** Instant specification fails to identify structural/functional correlation which is definitive of the claimed fragment. Although instant claims recite operable activity, the claims do not recite structural limitation which correlates to said activity, because the structure of the claimed fragment is not described. There is no written description of said fragment. The issue is not whether one of ordinary skill in the art can test fragments for the recited activities, but the innumerable number of fragments that are encompassed by the claims.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA

molecules, (in the instant case fragments of IL-1 epsilon which retain the recited activities), usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore, Applicants are not enabled or provide written description for a fragment of the claimed polypeptide which retains the recited activities.

New Rejections.

5. The indicated allowability of claims 28, 30 are withdrawn in view of the following new rejections.

Claim rejections-35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claims 21, 23, 25, 26, 28-29, 31-33, 35-38, 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising a Polynucleotide that encodes the polypeptide set forth in SEQ ID NO: 8, does not reasonably provide enablement for an isolated polynucleotide encoding the polypeptide set forth in SEQ ID NO:6 or 13 or fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and *use* the invention commensurate in scope with these claims.

Instant claims 21 is draw to an isolated nucleic acid which encodes the polypeptide of SEQ ID NO:6, 8 or 13 . The specification describes the polypeptide comprising the amino acid sequence set forth in SEQ ID No: 8, encoded by the nucleic acid of SEQ ID NO:7, as human IL-1 epsilon, (page 5, lines 19-40). The specification also discloses that human IL-1 epsilon polypeptide were transfected into COS cells and showed that conditioned medium containing human IL-1 epsilon activated IKIBα and p38 MAP kinase phosphorylation in number of human cell lines including Human Foreskin Fibroblasts (HFF) and Human Umbilical Vein Endothelial cells, (see Example III on page 48). The specification also demonstrates that HFF cells incubated in conditioned medium from cells that had been transfected with IL-1 epsilon exhibited a two fold increase in cell surface expression of ICAM-1 levels, (see page 50, lines 6-12). Therefore, it is interpreted that the human IL-1 epsilon polypeptide used in the above experiments is the one comprising the amino acid sequence set forth in SEQ ID NO:8. Instant specification describes the nucleic acid of SEQ ID NO:5 as a human DNA encoding a portion of a protein with high homology to mouse IL-1 epsilon in the same region, (see page 4, lines 33-39), and the nucleic acid of SEQ ID NO:12 as a single nucleotide polymorphism of the human IL-1 epsilon gene. However, instant specification does not show that neither the polypeptide of SEQ ID No: 6 nor 13 exhibits any of the activities demonstrated for the polypeptide of SEQ ID NO:8. Therefore, while instant specification discloses that the polypeptide of SEQ ID NO:8 exhibits the biological activities mentioned above, it does not disclose any activities for the polypeptides of SEQ ID Nos: 6 and 13.

Instant specification does not disclose an activity for the polypeptide of SEQ ID No: 6 or 13, and one of ordinary skill in the art would not reasonably predict that these proteins would exhibit the

same activities demonstrated for the polypeptide of SEQ ID NO:8, given the fact that not all of the members of the IL-1 family display similar biological activities. Applicants have not shown that the polypeptide of SEQ ID NO:6, which comprises only the last 70 amino acids residues of SEQ ID NO:8, would display the same activities as that of the polypeptide of SEQ ID NO:8. Neither do Applicants show whether the polypeptide of SEQ ID NO:13 which is encoded by a single nucleotide polymorphism (SNP) of the polynucleotide of SEQ ID NO:7, displays the same activities of the polypeptide of SEQ ID NO:8. The polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:12 is an SNP which encodes a substitution of a glutamine for an arginine at position 12 of the polypeptide of SEQ ID NO:8. However, Applicants have not shown the significance of this change. Many diseases are known to be caused by SNPs, which makes the identification of SNPs an important endeavor. However, Applicants must attach a significance to the fact that the polypeptide of SEQ ID NO:13 is encoded by an SNP of the polynucleotide of SEQ ID NO:7. Does the SNP present a significant change in the biological activities of that of SEQ ID NO:8, or do the two proteins display similar activities? Furthermore, one of ordinary skill in the art would not know how to use the polypeptide of SEQ ID NO: 6 or 13, because applicants do not disclose any activities for them. As such, claims drawn to a nucleic acid encoding the polypeptide of SEQ ID NO:6 or 13 are not enabled, because Applicants do not provide activities for these polypeptides, and thus, the skilled artisan would not know how to use said polypeptide.

Conclusion

7. Claims 24, 27, 30, 34 and 39 are allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday, Wednesday-Thursday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
04 February 2003

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